Research Involving Animals

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1. Introduction

The DOD definition of animal is "Any live nonhuman vertebrate". Institutions funded by Department of Defense agencies using animals in support of programs to conduct research, product development, testing and education projects must provide all information outlined in this appendix to their DOD program manager for DOD review and approval. This required information must be addressed in a proposal appendix entitled "Research Involving Animals." This requirement also applies to all subcontractors using animals in support of DOD funded projects or programs.

The DOD policy and requirements for the use of animals in DOD-funded research, development, testing and evaluation are listed in Department of Defense Directive 3216.1, dated April 17, 1995. These requirements may differ from those of other funding agencies.

Questions concerning animal use and review should be directed to MCMR-ZB-QA:

Phone: 301-619-2144
Fax: 301-619-4165
Mail: U.S. Army Medical Research and Materiel Command
ATTN: MCMR-ZB-QA
504 Scott Street
Fort Detrick, MD 21702-5012

2. Alternatives to Painful Procedures:

The USDA definition of painful procedure is "any procedure that would reasonably be expected to cause more than slight or momentary pain and/or distress in a human being to which that procedure is applied." Provide a narrative description of the methods and sources the Principal Investigator used to determine that alternatives were not available to the painful/distressful procedure or procedures used in the experiment, including those procedures in which pain/distress is alleviated (e.g., the Altweb (Johns Hopkins Center for Alternatives to Animal Testing), MEDLINE, Life Sciences Abstracts, AGRICOLA, and BIOSIS). The narrative must include: databases searched or other sources consulted, date of the search, years covered by the search, key words and/or search strategy used, and a discussion of what alternatives were considered but not used. If applicable, state the appropriate federal law or legal guidance that requires the specific testing procedures covered in the proposal to which alternative testing methods are not allowed.

3. Literature Search for Unnecessary Duplication:

Provide the following information describing your database search to ensure this proposal is not duplicating previous experiments: databases searched, keywords or search strategy used, period of search, and date search was performed. At least two databases must be searched: the Biomedical Research Database (BRD) at http://www.scitechweb.com/acau/brd/ and one of the following databases: Computer

Retrieval of Information of Scientific Projects (CRISP) at http://www.crisp.cit.nih.gov/ or the Federal Research in Progress (FEDRIP) at http://grc.ntis.gov. Additional searches in databases specific to the area of research performed in the proposal are highly recommended.

4. Rationale for Using Animals:

Provide a justification for using animals in the proposed research. State alternatives to animal use that you considered and explain why these alternatives cannot be used to obtain the research objectives (e.g., computer modeling, cell cultures).

5. Species Identification and Rationale:

Provide the species name and if applicable the strain, stock or breed of animals used in the proposal. State the strain or stock if mice, rats or guinea pigs are used. State the breed if dogs, cats or rabbits are used. Provide a justification for using this particular animal model to include a discussion of the unique morphological and physiological characteristics of this animal model which makes it the best choice for this project.

6. Number of Animals Used:

List the number of: experimental groups, animals in each group and the total animals used by species. Also, using the USDA definition of "painful procedure" presented in paragraph 2 above:

a. State the common names and number of animals in this proposal which will experience **no more than slight** or momentary pain or distress.

b. State the common names and numbers of animals in this proposal which will experience pain or distress that **will be relieved** with anesthetics and/or analgesics.

c. State the common names and numbers of animals in this proposal which will experience pain or distress that **will not be relieved** with anesthetics and/or analgesics.

7. Rationale for the Number of Animals Required:

List the total number of animals used in this proposal and the size of the experimental groups. Include animals necessary for controls, technique development, expected losses, etc. Describe the statistical methodology used to determine that at least the minimum number of animals is used to obtain valid scientific results. State the statistical test(s) planned or describe the strategy intended to evaluate the data. If applicable, state the appropriate CFR or federal reference which requires specific group sizes and total number of animals be used in an experiment or test.

8. Experimental Design:

Outline the scientific plan and direction of experimentation. Provide a complete description of the experimental design of the project to include a summary table of experimental groups and a flowchart indicating sequence of experimental events. Describe the experimental design of each experiment separately if several experiments or sequential studies are included in the proposal.

9. Technical Methods:

State frequency of animal observation once experimental procedures start and describe health status assessment criteria used. Provide a complete description of all procedures the animals will experience to include:

a. surgical procedures
b. biosamples (i.e., frequency, volume, harvest site, and collection method)
c. adjuvants (if using Complete Freund's Adjuvant and/or *in vivo* production of monoclonal antibodies, provide a scientific justification and state what alternatives you considered and why they were not used)
d. tissue sampling for DNA analysis (i.e., age of sampling, amount of tissue taken, anesthetic use)
e. injections (i.e., agent, dosage, route, and anatomical site of administration)
f. prolonged restraint (additionally, justification for its use)
g. food or water restriction (additionally, justification for its use)
h. multiple major survival surgeries on the same animal (additionally, justification for its use)

10. Anesthesia/Analgesia/Tranquilization:

Describe the methods or strategies planned to effectively relieve pain and distress. If drugs are used for anesthesia, analgesia or tranquilization list the drug: name, dosage, frequency, route, and anatomical site of administration. List the observation criteria utilized to determine if the animals are experiencing pain and/or distress. Provide justification for using the following agents or procedures if they are used in the proposal: neonatal hypothermia, chloral hydrate, alpha-chloralose, ether or urethane. If applicable, provide an explanation for withholding anesthetic/analgesic agents from animals that will experience a painful or distressful procedure yet not receive anesthesia or analgesia.

11. Study Endpoint:

State the projected study endpoint for the animals (e.g., recovery, euthanasia). Define specific health assessment criteria used to determine early study endpoints and/or indication for euthanasia (e.g., percentage of weight loss, tumor size, number of abdominal taps, abdominal distention, anorexia, decreased activity, ruffled fur).

12. Euthanasia or Final Disposition:

Describe the method of euthanasia by agent, dosage, route, and anatomical site of administration. State the final disposition of the animals if they are not euthanized. If

administration of carbon dioxide is the proposed method of euthanasia, indicate how death will be confirmed.

13. Institutional Animal Care and Use Committee(s) (IACUC) Approvals:

Provide documentation of IACUC protocol review and approval in the form of a letter on institutional stationery signed by the IACUC chair or the IACUC administrator from the facility where the animal research is performed--to include any subcontracted facilities if applicable. Evidence of IACUC review and approval may follow proposal submission, but must be provided prior to DOD animal proposal approval.

14. U.S. Department of Agriculture (USDA) Animal and Plant Health Inspection Service Animal Care Inspection Report:

Include a copy of the most recent annual USDA Facility Inspection Report for any and all facilities where animal research is performed to include any subcontracted facility or facilities.

15. Qualifications:

List by name all personnel working with animals under this proposal and all procedures, manipulations and observations each individual will perform. Provide each individual's training, experience, and qualifications to perform these duties (e.g., surgery, euthanasia, pre- and post-operative care, injections, phlebotomy, restraint). Training citations should include all institutional courses provided to comply with CFR 9, paragraph 2.32. Qualifications should include educational degrees.

16. Accreditation:

Provide the following documents for each facility where the animal research will be conducted, if applicable:

a. A copy of an Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC) letter confirming the institution's accreditation.

b. A copy of the current Institutional Letter of Assurance of Compliance with the "Public Health Service Policy on Humane Care and Use of Laboratory Animals," revised September 1986.

c. In the event that items 16.a. and 16.b do not apply to your institution, provide a statement signed by the Institutional Official that the care and use of animals will be performed according to the National Research Council 1996 "Guide for the Care and Use of Laboratory Animals" and applicable Federal regulations.

17. Principal Investigator Assurances:

The law specifically requires several written assurances from the P.I. Please read and sign the assurances as indicated (this page may be photocopied and signed).

As the Principal Investigator on this protocol, I acknowledge my responsibilities and provide assurances for the following:

A. Painful Procedures: I assure that discomfort and injury to animals will be limited to that which is unavoidable in the conduct of scientifically valuable research and that analgesic, anesthetic, and/or tranquilizing drugs will be used where indicated and appropriate to minimize pain and/or distress to animals.

B. Animal Use: The animals authorized for use in this protocol will be used only in the activities and in the manner described herein, unless a modification is specifically approved by the IACUC and the U.S. Army Medical Research and Materiel Command prior to its implementation.

C. Duplication of Effort: I have made a reasonable, good faith effort to ensure that this protocol is not an unnecessary duplication of previous experiments.

D. Statistical Assurance: I assure that I have consulted with a qualified individual who evaluated the experimental design with respect to the statistical analysis, and that the minimum number of animals needed for scientific validity will be used.

E. Training: I verify that the personnel performing the animal procedures/manipulations/observations described in this protocol are technically competent and have been properly trained to ensure that no unnecessary pain or distress will be caused to the animals as a result of the procedures/manipulations.

F. Responsibility: I acknowledge the inherent moral, ethical and administrative obligations associated with the performance of this animal use protocol, and I assure that all individuals associated with this project will demonstrate a concern for the health, comfort, welfare, and well-being of the research animals. Additionally, I pledge to implement animal use alternatives where feasible, and conduct humane and lawful research.

G. Scientific Review: This proposed animal use protocol has received appropriate peer scientific review, and is consistent with good scientific research practice.

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(Principal Investigator Printed Name) (Principal Investigator Signature and Date)

NOTE: A site visit will be conducted by the USAMRMC Animal Care and Use Review Officer or designees of sites using nonhuman primates, dogs, cats or marine mammals in the proposal, or where a site visit is deemed warranted.